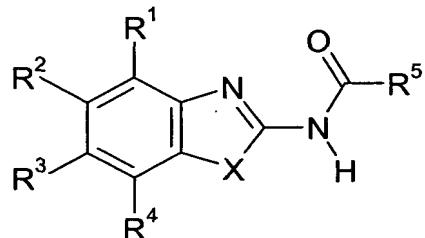


We claim:

1. A compound of formula I,



5

I

wherein:

R¹ and R⁴ are each, independently,

- 10 H;
 C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, each of which is optionally substituted one or more times by F, OH, C₁-C₈-alkoxy, C₁-C₈-alkylmercapto, -CN, COOR⁶, CONR⁷R⁸, phenyl or heteroaryl, wherein the phenyl and heteroaryl are each independently optionally substituted one or more times by halogen, -CN, C₁-C₃-alkyl, C₁-C₃-alkoxy or CF₃;
- 15 phenyl or heteroaryl, each of which is optionally substituted one or more times by halogen, -CN, C₁-C₃-alkyl, C₁-C₃-alkoxy or CF₃;
 COR⁹;
 CONR¹⁰R¹¹;
- 20 COOR¹²;
 CF₃;
 halogen;
 -CN;
 NR¹³R¹⁴;
- 25 OR¹⁵;
 S(O)_mR¹⁶;
 SO₂NR¹⁷R¹⁸; or

NO₂;

R² and R³ are each, independently,

H;

5 halogen;

-CN;

C₁-C₁₀-alkyl, optionally substituted one or more times by OH, phenyl, or heteroaryl;

OH;

10 C₁-C₁₀-alkoxy;

phenoxy;

S(O)_mR¹⁹;

CF₃;

NO₂;

15 C₁-C₁₀-alkylamino;

di(C₁-C₁₀-alkyl)amino;

(C₁-C₆-alkyl)-CONH-;

phenyl-CONH- or phenyl-SO₂-O-, wherein the phenyl is optionally substituted one or more times by halogen, -CN, methyl or methoxy;

20 C₁-C₆-alkyl-SO₂-O-;

(C₁-C₆-alkyl)-CO-, wherein the C₁-C₆-alkyl is optionally substituted one or more times by F, di(C₁-C₃-alkyl)amino, pyrrolidinyl or piperidinyl; or

phenyl-CO-, wherein the phenyl is optionally substituted one or more times by C₁-C₃-alkyl, halogen or methoxy;

25

R⁵ is Ar or Hetar, each of which is optionally substituted one or more times by

halogen;

-CN;

NH₂;

30 C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl, C₂-C₁₀-alkynyl, C₁-C₁₀-alkoxy, C₁-C₁₀-alkylamino or di(C₁-C₁₀-alkyl)amino, wherein the alkyl, alkenyl, alkynyl

and alkoxy are each independently optionally substituted one or more times by F, OH, C₁-C₈-alkoxy, aryloxy, C₁-C₈-alkylmercapto, NH₂, C₁-C₈-alkylamino or di(C₁-C₈-alkyl)amino; C₃-C₅-alkandiyl;

5 phenyl; •

heteroaryl;

aryl-substituted or heteroaryl-substituted C₁-C₄-alkyl;

CF₃;

NO₂;

10 OH;

phenoxy;

benzyloxy;

(C₁-C₁₀-alkyl)-COO-;

S(O)_mR²⁰;

15 SH;

phenylamino;

benzylamino;

(C₁-C₁₀-alkyl)-CONH-;

(C₁-C₁₀-alkyl)-CO-N(C₁-C₄-alkyl)-;

20 phenyl-CONH-;

phenyl-CO-N(C₁-C₄-alkyl)-;

heteroaryl-CONH-;

heteroaryl-CO-N(C₁-C₄-alkyl)-;

(C₁-C₁₀-alkyl)-CO-;

25 phenyl-CO-;

heteroaryl-CO-;

CF₃-CO-;

-OCH₂O-;

-OCF₂O-;

30 -OCH₂CH₂O-;

-CH₂CH₂O-;

- COOR²¹;
 CONR²²R²³;
 C(NH)-NH₂;
 SO₂NR²⁴R²⁵;
- 5 R²⁶SO₂NH-; R²⁷SO₂N(C₁-C₆-alkyl)-; or
 a residue of a saturated or unsaturated aliphatic, monocyclic 5-membered to 7-membered heterocycle containing 1, 2 or 3 heteroatoms selected from the group consisting of N, O and S, wherein the heterocycle is optionally substituted one or more times by halogen, C₁-C₃-alkyl, C₁-C₃-alkoxy, OH, oxo or CF₃, and the heterocycle is optionally condensed to the group Ar or the group Hetar; wherein all aryl, heteroaryl, phenyl, aryl-containing, heteroaryl-containing and phenyl-containing groups, which are optionally present in the said substituents of the said group Ar or the said group Hetar, can be substituted by one or more substituents selected from the group consisting of halogens, -CN, C₁-C₃-alkyl, OH, C₁-C₃-alkoxy, and CF₃;
- 10 R⁶ is H;
- 15 C₁-C₁₀-alkyl, optionally substituted one or more times by F, C₁-C₈-alkoxy or di(C₁-C₈-alkyl)amino; aryl-(C₁-C₄-alkyl)- or heteroaryl-(C₁-C₄-alkyl)- either of which is optionally substituted one or more times by halogen, C₁-C₄-alkyl, C₁-C₄-alkoxy or di(C₁-C₆-alkyl)amino;
- 20 R⁷ is H; C₁-C₁₀-alkyl, optionally substituted one or more times by F, C₁-C₈-alkoxy, di(C₁-C₈-alkyl)amino or phenyl; or phenyl, indanyl or heteroaryl, each of which is optionally substituted one or
- 25 more times by halogen, -CN, C₁-C₃-alkyl, C₁-C₃-alkoxy or CF₃;

R⁸ is H or C₁-C₁₀-alkyl;

R⁹ is C₁-C₁₀-alkyl, optionally substituted one or more times by F, C₁-C₄-alkoxy or di(C₁-C₃-alkyl)amino; or

5 phenyl or heteroaryl, each of which is optionally substituted one or more times by C₁-C₃-alkyl, C₁-C₃-alkoxy, halogen, -CN or CF₃;

R¹⁰, independently from R⁷, is R⁷;

10 R¹¹, independently from R⁸, is R⁸;

R¹², independently from R⁶, is R⁶;

R¹³ is H;

15 C₁-C₆-alkyl; or
phenyl, benzyl, heteroaryl, (C₁-C₆-alkyl)-CO-, phenyl-CO-, or heteroaryl-CO-,
each of which is optionally substituted one or more times by halogen, -CN, C₁-C₃-alkyl, C₁-C₃-alkoxy or CF₃;

20 R¹⁴, independently from R¹³, is R¹³;

R¹⁵ is H;

C₁-C₁₀-alkyl;

(C₁-C₃-alkoxy)-C₁-C₃-alkyl-;

25 benzyl, phenyl or heteroaryl, each of which is optionally substituted one or
more times by halogen, -CN, C₁-C₃-alkyl, C₁-C₃-alkoxy or CF₃;

R¹⁶ is C₁-C₁₀-alkyl, optionally substituted one or more times by F, OH, C₁-C₈-alkoxy,
aryloxy, C₁-C₈-alkylmercapto, C₁-C₈-alkylamino or di(C₁-C₈-alkyl)amino;

30 CF₃; or

phenyl or heteroaryl, each of which is optionally substituted one or more times by halogen, -CN, C₁-C₃-alkyl, C₁-C₃-alkoxy or CF₃;

R¹⁷, independently from R⁷, is R⁷;

5

R¹⁸, independently from R⁸, is R⁸;

R¹⁹, independently from R¹⁶, is R¹⁶;

10 R²⁰, independently from R¹⁶, is R¹⁶;

R²¹, independently from R⁶, is R⁶;

R²², independently from R⁷, is R⁷;

15

R²³, independently from R⁸, is R⁸;

R²⁴, independently from R⁷, is R⁷;

20 R²⁵, independently from R⁸, is R⁸;

R²⁶, independently from R¹⁶, is R¹⁶;

R²⁷, independently from R¹⁶, is R¹⁶;

25

R³⁰ is H;

C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, each of which is optionally substituted one or more times by F, OH, C₁-C₈-alkoxy, C₁-C₈-alkylmercapto, -CN, COOR³¹, CONR³²R³³, NR³⁴R³⁵, (C₁-C₈-alkyl)-CONH-, (C₁-C₈-alkoxy)-CONH-, benzyloxy-CONH-, phenyl or heteroaryl, wherein the phenyl and

30

heteroaryl are each independently optionally substituted one or more times by halogen, -CN, C₁-C₃-alkyl, C₁-C₃-alkoxy or CF₃; or phenyl or heteroaryl, each of which is optionally substituted one or more times by halogen, -CN, C₁-C₃-alkyl, C₁-C₃-alkoxy or CF₃;

5

R³¹, independently from R⁶, is R⁶;

R³², independently from R⁶, is R⁶;

10 R³³, independently from R⁶, is R⁶;

R³⁴, independently from R⁶, is R⁶;

R³⁵, independently from R⁶, is R⁶;

15

X is NR³⁰, S, O, CH=CH, N=CH or CH=N;

heteroaryl is a residue of a 5-membered to 10-membered, aromatic, monocyclic or bicyclic heterocycle containing one or more heteroatoms selected from the group

20 consisting of N, O and S;

the group Hetar is a residue of a 5-membered to 10-membered, aromatic, monocyclic or bicyclic heterocycle containing one or more heteroatoms selected from the group consisting of N, O and S;

25

aryl is phenyl, naphth-1-yl or naphth-2-yl;

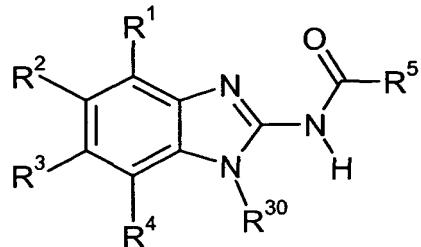
the group Ar is phenyl, naphth-1-yl or naphth-2-yl; and

30 m is 0, 1 or 2;

or a stereoisomer or a mixture of stereoisomers thereof in any ratio, or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 of formula Ia

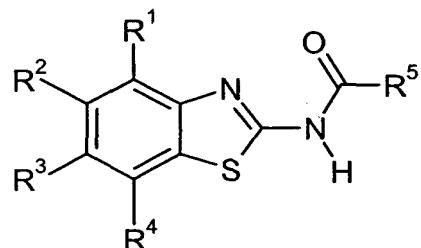
5



Ia

wherein R³⁰ is methyl.

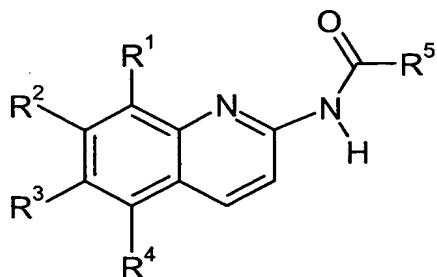
10 3. A compound according to claim 1 of formula Ic



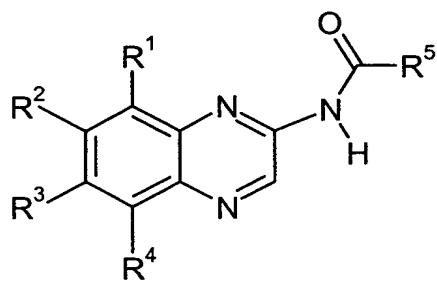
Ic

4. A compound according to claim 1 of formula Id

15



5. A compound according to claim 1 of formula Ie



5

Ie

6. A compound according to claim 1, wherein:

R¹ and R⁴ are each, independently,

H;

10 Halogen; or

C₁-C₄-alkyl;

and

R² and R³ are each, independently,

H;

15 Halogen; or

C₁-C₄-alkyl.

7. A compound according to claim 1, wherein:

R⁵ is phenyl or Hetar, each of which is optionally substituted one or more times by

20 halogen;

- CN;
- NH₂;
- C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, C₁-C₃-alkoxy, C₁-C₄-alkylamino or di(C₁-C₄-alkyl)amino, each of which is optionally substituted one or more times by F, C₁-C₃-alkoxy, C₁-C₃-alkylmercapto or NH₂;
- 5 C₃-C₅-alkandiyil;
- phenyl;
- heteroaryl;
- 10 phenyl-substituted or heteroaryl-substituted C₁-C₂-alkyl;
- CF₃;
- OH;
- (C₁-C₄-alkyl)-COO;
- S(O)_m-(C₁-C₄)-alkyl;
- 15 (C₁-C₄-alkyl)-CONH-;
- (C₁-C₄-alkyl)-CON(C₁-C₄-alkyl)-;
- (C₁-C₄-alkyl)-CO-;
- phenyl-CO-;
- heteroaryl-CO-;
- 20 CF₃-CO-;
- OCH₂O-;
- OCF₂O-;
- OCH₂CH₂O-;
- CH₂CH₂O-;
- 25 COO(C₁-C₆-alkyl);
- CONH₂;
- CONH(C₁-C₄-alkyl);
- CON(di(C₁-C₄-alkyl));
- C(NH)NH₂;
- 30 -SO₂NH₂;
- SO₂NH(C₁-C₄-alkyl);

-SO₂NH(phenyl);

-SO₂N(di(C₁-C₄-alkyl));

(C₁-C₄-alkyl)-SO₂NH-;

(C₁-C₄-alkyl)-SO₂N(C₁-C₄-alkyl)-; or

5 a residue of a saturated or unsaturated aliphatic, mononuclear 5-membered to 7-membered heterocycle containing 1, 2 or 3 heteroatoms selected from the group consisting of N, O and S, wherein the heterocycle is optionally substituted one or more times by halogen, C₁-C₃-alkyl, C₁-C₃-alkoxy, OH, oxo or CF₃, and the heterocycle is optionally condensed to the said phenyl or the said group Hetar;

10 wherein all heteroaryl, phenyl, heteroaryl-containing and phenyl-containing groups, which are optionally present in the said substituents of the said phenyl or the said group Hetar, can be substituted by one or more substituents selected from the group consisting of halogen, -CN, C₁-C₃-alkyl, OH, C₁-C₃-alkoxy, and CF₃.

15 8. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound according to claim 1 and a pharmaceutically acceptable carrier.

20 9. A method for the stimulation of the expression of endothelial NO synthase, in a patient in need thereof, comprising administering to the patient a pharmaceutically effective amount of a compound according to claim 1.

25 10. A method for the treatment of cardiovascular diseases, stable or unstable angina pectoris, coronary heart disease, Prinzmetal angina, acute coronary syndrome, heart failure, myocardial infarction, stroke, thrombosis, peripheral artery occlusive disease, endothelial dysfunction, atherosclerosis, restenosis, endothelial damage after PTCA, hypertension, essential hypertension, pulmonary hypertension, secondary hypertension, renovascular hypertension, chronic glomerulonephritis, erectile dysfunction, ventricular arrhythmia, diabetes, diabetes complications, nephropathy, retinopathy, angiogenesis, asthma bronchiale, chronic renal failure, cirrhosis of the

liver, osteoporosis, restricted memory performance or a restricted ability to learn, or for the lowering of cardiovascular risk of postmenopausal women or of women taking contraceptives, in a patient in need thereof, comprising administering to the patient a pharmaceutically effective amount of a compound according to claim 1.